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Arlington, VA 22202  
on September 4, 2001  
Date of Deposit

Carolyn Roberts

Name of applicant, assignee  
or Registered Representative

Signature

September 4, 2001

Date of Signature

Patent  
Case No. P-191

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Clark M. Whitehead et al. )  
Serial No.: 09/938,160 ) Examiner: Not Yet Assigned  
Filed: August 23, 2001 ) Art Unit: Not Yet Assigned  
For: METHODS FOR TREATMENT OF )  
SCLERODERMA )

INFORMATION DISCLOSURE STATEMENT

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

Pursuant to the obligation under 37 C.F.R. § 1.56 and in conformance with 37 C.F.R. §§ 1.97-1.99, Applicants hereby submit the following documents for consideration by the Examiner. A copy of each has been enclosed along with two copies of the PTO-1449 form.

U.S. Patents

<u>Patent No.</u>	<u>Date</u>	<u>Name</u>
3,031,450	April 24, 1962	Fischer et al.
3,161,654	December 15, 1964	Shen
3,312,730	April 4, 1967	Winter et al.
3,322,755	May 30, 1967	Roch et al.
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3,642,785	February 15, 1972	Shen et al.
3,647,858	March 7, 1972	Hinkley et al.
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5,298,525	March 29, 1994	Yoon et al.
5,401,774	March 28, 1995	Pamukcu et al.
5,470,873	November 28, 1995	Yoon
5,488,055	January 30, 1996	Kumar et al.
5,527,896	June 18, 1996	Wigler et al.
5,602,019	February 11, 1997	Beavo et al.
5,602,171	February 11, 1997	Tang et al.
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<u>Patent No.</u>	<u>Date</u>	<u>Name</u>
5,614,627	March 25, 1997	Takase et al.
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5,776,752	July 7, 1998	Beavo et al.
5,789,553	August 4, 1998	Beavo et al.
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5,852,035	December 22, 1998	Pamukcu et al.
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#### REMARKS

Applicants request that these references be made of record in this case, and that the Examiner indicate his review of these references by initialing and returning one copy of the PTO form enclosed.

This Information Disclosure Statement is being submitted before the mailing of the first Office Action on the merits pursuant to 37 C.F.R. § 1.97.

Respectfully submitted,



Robert W. Stevenson  
Reg. No. 31064  
Attorney for Applicants

Dated: September 4, 2001

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FORM PTO-1449

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LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE STATEMENT  
(use several sheets if necessary)

SERIAL NO.	09/938,160	CASE NO.
FILING DATE	AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
APPLICANT(S):	WHITEHEAD ET AL.	

REFERENCE DESIGNATION                    U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A1	3,031,450	4/24/62	Fischer et al.		
A2	3,161,654	12/15/64	Shen		
A3	3,312,730	4/4/67	Winter et al.		
A4	3,322,755	5/30/67	Roch et al.		
A5	3,325,358	6/13/67	Winter et al.		
A6	3,532,752	10/6/70	Shen		
A7	3,642,785	2/15/72	Shen et al.		
A8	3,647,858	3/7/72	Hinkley et al.		
A9	3,654,349	4/4/72	Shen et al.		
A10	3,692,651	9/19/72	Sletzinger et al.		
A11	3,692,825	9/19/72	Conn		
A12	3,737,455	6/5/73	Shen et al.		
A13	3,851,063	11/26/74	Shen et al.		

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EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
A14	EP 0 293 063 B1	3/18/92	EPO		
A15	EP 0 347 146 B1	9/1/93	EPO		
A16	EP 0 349 239 A2	1/3/90	EPO		
A17	EP 0 352 960 B1	10/26/94	EPO		
A18	EP 0 351 058 B1	6/2/93	EPO		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
A19	Ahmad F. et al., IL-3 ad IL-4 Activate Cyclic Nucleotide Phosphodiesterases 3 (PDE3) and 4 (PDE4) by Different Mechanisms in FDCP2 Myeloid Cells, <i>J. Immunology</i> Vol. 162, Part 8, pp. 4864-4875 (Apr 15 1999).	
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A21	Cooper N. et al., A comparison of the inhibitory activity of PDE4 inhibitors on leukocyte PDE4 activity in vitro and eosinophil trafficking in vivo, <i>British Journal of Pharmacology</i> (1999) 126, pp. 1863-1871.	
A22	Czirjak L. et al., Investigation of the alveolar macrophages and T lymphocytes in 15 patients with systemic sclerosis, <i>Clin Rheumatology</i> 1999; 18(5), pp. 357-363 (Abstract Only).	
A23	Danahay H. et al., PDE4 inhibition and a corticosteroid in chronically antigen exposed conscious guinea-pigs, <i>Clinical and Experimental Allergy</i> , 1998, Vol. 28, pp. 513-522.	
A24	Duggan, D.E. et al., Identification of the Biologically Active Form of Sulindac, <i>J. Pharm. &amp; Exper. Therap.</i> , Vol. 201, No. 1, pp.8-13 (1977).	

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A25	3,860,636	11/14/75	Shen et al.		
A26	4,402,979	9/6/83	Shen et al.		
A27	4,307,114	12/22/81	Dvornik et al.		
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A30	4,880,810	11/14/89	Lowe, III		
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A32	5,298,525	3/29/94	Yoon et al.		
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A36	5,527,896	6/18/96	Wigler et al.		
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EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A43	Gantner F. et al., Characterization of the Phosphodiesterase (PDE) Pattern of in Vitro-Generated Human Dendritic Cells (DC) and the Influence of PDE Inhibitors on DC Function, Pulmonary Pharmacology & Therapeutics (1999) 12, pp. 377-386.
	A44	Gantner F. et al., In vitro differentiation of human monocytes to macrophages: change of PDE profile and its relationship to suppression of tumour necrosis factor-α release by PDE inhibitors, British Journal of Pharmacology (1997) 121, pp. 221-231.
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	A46	Germain N. et al., Selective phosphodiesterase inhibitors modulate the activity of alveolar macrophages from sensitized guinea-pigs, Eur. Respir. J. 1998;12, pp. 1334-1339.
	A47	Giembycz, M.A., Phosphodiesterase 4 Inhibitors and the Treatment of Asthma, Drugs 2000 Feb; 59(2), pp. 193-212.
	A48	Gonzaga, R.A.F. et al., The Lancet, 3/30/85, p. 751.

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A53	5,776,752	7/7/98	Beavo et al.		
A54	5,789,553	8/4/98	Beavo et al.		
A55	5,798,374	8/25/98	Tang et al.		
A56	5,800,987	9/1/98	Beavo et al.		
A57	5,852,035	12/22/98	Pamukcu et al.		
A58	5,858,694	1/12/99	Piazza et al.		
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A69	Hollander AP et al., Expression of hypoxia-inducible factor 1 alpha by macrophages in the rheumatoid synovium: implications for targeting of therapeutic genes to the inflamed joint, Arthritis Rheum. 2001 Jul; 44(7): 1540-4 (Abstract Only).	
A70	Imahashi K. et al., Type IV Phosphodiesterase Inhibitor Suppresses Insulin-Dependent Myocardial Glucose Uptake, Clin Exp Pharmacol Physiol 2001 Apr;28(4), pp. 290-291 (Abstract Only).	
A71	Ishikawa O. et al., Macrophage infiltration in the skin of patients with systemic sclerosis, J. Rheumatology 1992 Aug; 19(8), pp. 1202-1206 (Abstract Only).	
A72	Kapur S. et al., Expression of Nitric Oxide Synthase in Skeletal Muscle, Diabetes, Vol. 46, Nov. 1997, pp. 1691-1700.	

EXAMINER	DATE CONSIDERED

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SERIAL NO.

09/938,160

CASE NO.

P-191

**LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE STATEMENT**  
(use several sheets if necessary)

FILING DATE

AUGUST 23, 2001

GROUP ART UNIT  
NOT YET ASSIGNED

APPLICANT(S): WHITEHEAD ET AL.

**REFERENCE DESIGNATION****U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A73	5,885,834	3/23/99	Epstein		
A74	5,902,827	5/11/99	Pamukcu et al.		
A75	5,922,595	7/13/99	Fisher et al.		
A76	5,942,520	8/24/99	Pamukcu et al.		
A77	5,948,911	9/7/99	Pamukcu et al.		
A78	5,958,982	9/28/99	Pamukcu et al.		
A79	5,990,117	11/23/99	Pamukcu et al.		
A80	5,998,463	12/7/99	Hulin et al.		
A81	6,008,215	12/28/99	Flockerzi		
A82	6,015,677	1/18/00	Beavo et al.		
A83	6,034,099	3/7/00	Pamukcu et al.		
A84	6,037,345	3/14/00	Pamukcu et al.		
A85	6,046,199	4/4/00	Pamukcu et al.		

**FOREIGN PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES	TRANSLATION NO
A86	SHO 61-106521	5/24/86	Japan			
A87	WO 01/04099 A1	1/18/01	PCT			
A88	WO 00/12501	3/9/00	PCT	→ US 6,436,952		
A89	WO 00/26201	5/11/00	PCT	→ US 6,376,493		
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EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
A91	Kelly J. et al., Characterization of phosphodiesterase 4 in guinea-pig macrophages: multiple activities, association states and sensitivity to selective inhibitors, British Journal of Pharmacology (1998) 124, PP. 129-140.	
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A93	Kumar A. et al., Analgesic and anti-inflammatory effects of phosphodiesterase inhibitors, Indian J Exp Biol 2000 Jan;38(1), pp. 26-30 (Abstract Only)	
A94	Lee MS et al., A comparative immunohistochemical study of lichen planus and discoid lupus erythematosus, Australas J. Dermatol. 1996 Nov.; 37(4): 188-92 (Abstract Only).	
A95	McPherson M.A. et al., A cyclic nucleotide PDE5 inhibitor corrects defective mucin secretion in submandibular cells containing antibody directed against the cystic fibrosis transmembrane conductance regulator protein, FEBS Letters 464 (1999), pp. 48-52.	
A96	Mery P.F. et al., Erythro-9-(2-hydroxy-3-nonyl)adenine inhibits cyclic GMP-stimulated phosphodiesterase in isolated cardiac myocytes, Mol. Pharmacology 1995 Jul;48(1), pp. 121-130 (Abstract Only)	

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EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A97	6,046,206	4/4/00	Pamukcu et al.		
A98	6,046,216	4/4/00	Piazza et al.		
A99	6,060,477	5/9/00	Piazza et al.		
A100	6,066,634	5/23/00	Sperl et al.		
A101	6,069,240	5/30/00	Wigler et al.		
A102	6,071,934	6/6/00	Sperl et al.		
A103	6,077,842	6/20/00	Pamukcu et al.		
A104	6,080,540	6/27/00	Wigler et al.		
A105	6,080,742	6/27/00	Germann et al.		
A106	6,080,772	6/27/00	Tang et al.		
A107	6,100,025	8/8/00	Wigler et al.		
A108	6,107,295	8/22/00	Rochus et al.		
A109	6,124,303	9/26/00	Pamukcu et al.		

**FOREIGN PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES    NO
A110	WO 00/26208	5/11/00	PCT		
A111	WO 00/27861	5/18/00	PCT		
A112	WO 00/42017	7/20/00	PCT		
A113	WO 00/42018	7/20/00	PCT		
A114	WO 00/42019	7/20/00	PCT		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages; etc.)	
A115	Méry, Pierre-François et al., EHNA as an Inhibitor of PDE2: A Pharmacological and Biochemical Study in Cardiac Myocytes, Phosphodiesterase Inhibitors (1996), pp. 81-88.	
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A117	Niebauer J. et al., Local L-Arginine Delivery After Balloon Angioplasty Reduces Monocyte Binding and Induces Apoptosis, Circulation 1999;100, pp. 1830-1835.	
A118	Odoux C. et al., Endothelin-1 secretion by alveolar macrophages in systemic sclerosis, Am. J. Respir. Crit. Care Med. 1997 Nov;156(5), pp. 1429-1435 (Abstract Only).	
A119	Ostensen M. et al., Nonsteroidal anti-inflammatory drugs in systemic lupus erythematosus, Lupus (2001) 10, pp. 135-139.	
A120	Piazza G.A. et al., Antineoplastic Drugs Sulindac Sulfide and Sulfone Inhibit Cell Growth by Inducing Apoptosis, Cancer Research 55, Jul 15 1995, pp. 3110-3116.	

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**REFERENCE DESIGNATION U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A121	6,133,271	10/17/00	Pamukcu et al.		
A122	6,143,746	11/7/00	Daugan et al.		
A123	6,143,759	11/7/00	Flockerzi		
A124	6,143,765	11/7/00	Tang et al.		
A125	6,143,777	11/7/00	Jonas et al.		
A126	6,169,090	1/2/01	Dyke et al.		
A127	6,174,884	1/16/01	Haning et al.		
A128	6,187,779	2/13/01	Pamukcu et al.		
A129	6,200,771	3/13/01	Liu et al.		
A130	6,200,980	3/13/01	Piazza et al.		
A131	6,207,666	3/27/01	Piazza et al.		
A132	6,211,177	4/3/01	Sperl et al.		
A133	6,211,220	4/3/01	Pamukcu et al.		

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EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
A134	WO 00/42034	7/20/00	PCT		
A135	WO 00/59890	10/12/00	PCT		
A136	WO 00/64424	11/2/00	PCT		
A137	WO 99/65880	11/23/99	PCT	→ US 6,417,188	
A138	WO 98/19679A1	5/14/98	PCT (Claims Only)		

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A142	Soh, Jae-Won et al., Protein Kinase G Activates the JNK1 Pathway via Phosphorylation of MEKK1, The Journal of Biological Chemistry, Vol. 276, No. 19, pp. 16406-16410 (2001).
A143	Thompson, W.J. et al., Exisulind Induction of Apoptosis Involves Guanosine 3',5'-Cyclic Monophosphate Phosphodiesterase Inhibition, Protein Kinase G Activation, and Attenuated β-Catenin, Cancer Research 60, pp. 3338-3342, July 1, 2000.
A144	Tien, Xiao-Ying, et al., Activation of the Cystic Fibrosis Transmembrane Conductance Regulator by cGMP in the Human Colonic Cancer Cell Line, Caco-2, The Journal of Biological Chemistry, Vol. 269, No. 1, pp. 51-54 (1994).

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A145	6,232,312	5/15/01	Pamukcu et al.		
A146	6,235,742	5/22/01	Bell et al.		
A147	6,235,776	5/22/01	Pamukcu et al.		
A148	6,235,782	5/22/01	Pamukcu et al.		
A149	6,239,136	5/29/01	Pamukcu et al.		
A150	6,251,904	6/26/01	Bunnage et al.		
A151	6,255,303	7/3/01	Sterk et al.		
A152	6,255,456	7/3/01	Fisher et al.		
A153	6,258,833	7/10/01	Martins et al.		
A154	6,268,372	7/31/01	Pamukcu et al.		

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A155	WO 98/17668	4/30/98	PCT	→ US 6,130,223	
A156	WO 98/14448	4/9/98	PCT	→ US 6,265,577	
A157	WO 98/06722	2/19/98	PCT	→ US 6,110,920	
A158	WO 97/24334	7/10/97	PCT	→ US 6,166,219	
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A160	Tsukahara T et al., Cytophagic histiocytic panniculitis in systemic lupus erythematosus, Hiroshima J. Med. Sci., 1995 Mar; 44(1): 13-6 (Abstract Only).	
A161	Waddel W. R. et al., Sulindac for Polyposis of the Colon, The American Journal of Surgery, Vol. 157, Jan. 1989, pp. 175-179.	
A162	Waddel W. R. et al., Sulindac for Polyposis of the Colon, Journal of Surgical Oncology, 24: pp. 83-87 (1983).	
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A164	Wilder R.L. et al., Hormonal regulation of tumor necrosis factor-alpha, interleukin-12 and interleukin-10 production by activated macrophages. A disease-modifying mechanism in rheumatoid arthritis and systemic lupus erythematosus?, Ann. NY Acad. Sci 1999 June 22;876, pp. 14-31 (Abstract Only).	

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## **FOREIGN PATENT DOCUMENTS**

FOREIGN PATENT DOCUMENTS						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES	NO
	A165 WO 97/03675	2/6/97	PCT			
	A166 WO 94/29277	11/22/94	PCT			
	A167 WO 93/07149	4/15/93	PCT			

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